US005476659A

# United States Patent [19]

Goodman et al.

[11] Patent Number: 5,476,659

[45] Date of Patent: Dec. 19, 1995

[54] **CANCEROUS B CELL TREATMENT USING SUBSTITUTED NUCLEOSIDE DERIVATIVES**

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[21] Appl. No.: **151,142**

[22] Filed: **Nov. 12, 1993**

**Related U.S. Application Data**

[63] Continuation-in-part of Ser. No. 975,830, Nov. 13, 1992, abandoned, which is a continuation-in-part of Ser. No. 945,215, Sep. 15, 1992, Pat. No. 5,317,013, which is a division of Ser. No. 562,101, Aug. 2, 1990, Pat. No. 5,147,636, which is a division of Ser. No. 361,974, Jun. 9, 1989, Pat. No. 4,948,730, which is a division of Ser. No. 14,618, Feb. 13, 1987, Pat. No. 4,849,411, which is a continuation of Ser. No. 546,679, Nov. 1, 1983, Pat. No. 4,643,992, which is a continuation-in-part of Ser. No. 439,846, Nov. 9, 1982, Pat. No. 4,539,205.

[51] **Int. Cl.**[6] ..... **A61K 39/39**; A61K 31/70; C12N 5/06; C12N 5/08

[52] **U.S. Cl.** ..... **424/278.1**; 514/45; 514/908; 435/240.2

[58] **Field of Search** ..... 514/26, 34, 45, 514/171, 188, 885, 908; 424/178.1, 181.1, 278.1; 435/240.2

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[57] **ABSTRACT**

Processes for the killing of cancerous B cells, and particularly chronic lymphocytic leukemia (CLL) cells are disclosed. In one process, cancerous B cells that do not proliferate when contacted with an immune response-enhancing agent are contacted with an amount of such an agent sufficient to cause peripheral CLL cells to undergo blast transformation and proliferation. The contacted cells are then maintained for a time period sufficient for them to die from that contact. Further contacting of those cells with a cytotoxic amount of an anti-cancer drug or cytotoxic conjugate enhances the death of those cancer cells. In another process, peripheral CLL cells that proliferate on contact with an immune response-enhancing-agent are contacted with a proliferation-inducing amount of such an agent. The contacted cells are maintained for a time period sufficient to undergo blast transformation and proliferation, and the blasts are then contacted with a cytotoxic amount of an anti-cancer drug or cytotoxic conjugate and maintained.

**32 Claims, 7 Drawing Sheets**